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EXPLORATION FOR CASE TEACHING MODEL OF PHARMACEUTICAL SEPARATION ENGINEERING

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ABSTRACT

Objective: This study aims to cultivate students' comprehensive understanding and grasp of curriculum knowledge, example as pharmaceutical separation engineering course.

Materials and Methods: The case teaching model was explored in this paper. Taking the "extraction of penicillin" as an example, case teaching is designed and organized. After that, 1-4 Study Questions are put forward to guide and inspire students' broad thinking and improve their innovative ability. Results: Through case teaching, students not only learn to consult technical data, but also learn to design several effective separation and purification methods and process routes according to the property of penicillin, and the established process routes were analyzed and compared, so that the feasible, economical and optimal technology is found. Students' engineering ability and innovation ability can be improved and overall concept and consciousness can be cultivated.

Conclusion: This teaching model is really student-centered and provides an effective way to cultivate high-quality, innovative and practical pharmaceutical engineering talents.

KEYWORDS: case teaching; pharmaceutical separation engineering; student-centered; innovation ability ； practical ability

1. INTRODUCTION:

Pharmaceutical separation engineering is an important part of pharmaceutical engineering, and it is also an essential and critical link in the industrialization of pharmaceutical products[1-3]. Its main contents include material extraction, separation, purification, refinement and processing, covering a wide range and complicated knowledge points. Each knowledge point is not independent but also related to each other. Students have a good grasp of the principles and characteristics of various separation and purification methods, but lack of perceptual understanding. When it comes to practical problems such as process design according to the characteristics of separation products, students often fail to apply the theoretical knowledge to practice and lack of overall mastery of the curriculum and flexible application of various technologies. Therefore, the implementation of case teaching and the development of case teaching are the foothold to cultivate students' comprehensive understanding and grasp of curriculum knowledge. Case teaching can improve students' practical skills by discussing typical and pertinent cases in the limited time of classroom. In the process of teaching organization, teachers can put forward some questions for each case so that students can read cases and look up some information to the library. Therefore, it is feasible and advantageous to apply case teaching in classroom study of pharmaceutical separation engineering. At the same time, the concept of pharmaceutical engineering industrialization can also reflected in the teaching process. Case teaching is an effective way to cultivate high-quality, innovative and practical pharmaceutical engineering talents in pharmaceutical engineering education.

2. DESIGN AND ORIGINATION OF CASE TEACHING:

Case is a record of a complicated situation. A good case is a tool to introduce part of real scene into the classroom so that teachers and students can analyze and study it. It can make classroom discussions around the thorny problems that only exist in real scene4,5. Therefore, the selection of case is one of the main factors for the success of case teaching. In the teaching of pharmaceutical separation engineering, in order to achieve the teaching goal and avoid boring students with the tedious and complicated principles and the operation steps of talking about stratagems on paper, cases should be organically integrated into teaching so that students can understand and master them more easily, so as to achieve good teaching effect. Modern pharmaceutical industry production is a kind of business activity, and its core content is pharmaceutical products. For a general pharmaceutical product, its production route is not always the only one. In the actual sections for pharmaceutical production, for the choice of process routes, in addition to the technical feasibility, there are more reflects economic considerations, especially production costs, investment and return possibilities etc.

Taking the "extraction of penicillin" as an example, case teaching is organized as follows.

Known: State briefly what is known. This requires that students read the problem carefully and understand what information is given.

Find: State concisely what is to be determined.

Schematic and Given Data: Sketch the system to be considered. Decide whether a diagram is appropriate for the analysis. Label the system diagram with relevant information from the problem statement.

Record all material properties and other parameters that you are given or anticipate may be required for subsequent calculations. If appropriate, sketch diagrams that locate critical points and indicate the possible mode of failure.

The importance of good sketches of the system and diagrams cannot be overemphasized. They are often instrumental in enabling students to think clearly about the problem.

According to the known conditions, in this case teaching, three extraction processes of penicillin, i.e., liquid-liquid extraction processes, DBED precipitation processes and hollow fiber membrane processes were designed as follows. And the processes were shown in Figure 1, Figure 2 and Figure 3.

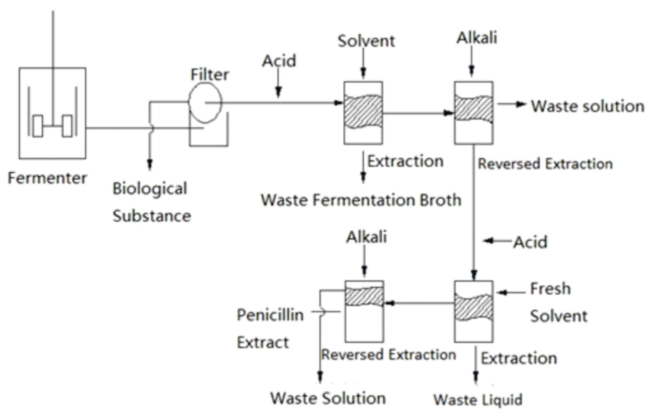

Figure1: Liquid-liquid extraction processes of penicillin

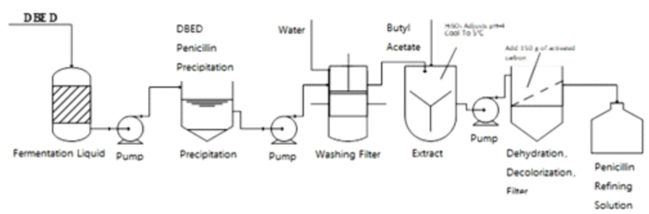

Figure 2: Extraction processes combined with DBED precipitation of penicillin

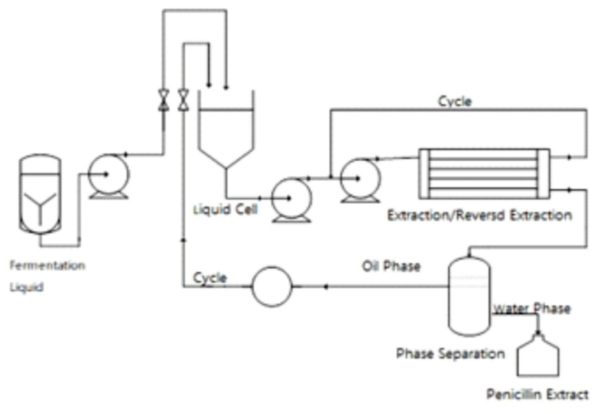

Figure 3: Extraction processes of penicillin with hollow fiber membrane component

Decisions: Record your choices and selections. Design problems will require you to make subjective decisions. Design decisions will involve selection of parameters such as geometric variables and types of materials. Decisions are individual choices.

Assumptions: To form a record of how you model the problem, list all simplifying assumptions and idealizations made to reduce it to one that is manageable. Sometimes this information can also be noted on the sketches. In general, once a design is complete, assumptions are still beliefs whereas decisions are true. Assumptions are theories about reality.

Analysis:

1) **Analysis of technological processes:** the process of liquid-liquid extraction was suitable to the continuous production, short production period, high yield, good product quality ,but large amount of the extractant was used, and ultracentrifugation equipment ,ventilation and fire-proof and explosion-proof measures were need , etc. while DBED precipitation penicillin method can be directly precipitated, there was high concentration of product, it can save a large amount of organic solvent than liquid-liquid extraction, and the stainless steel and ultracentrifugation equipment are also be saved, general equipment can be used, construction investment is saved. Hollow fiber membrane component is a new extraction process with synchronous separation and purification, compared to liquid-liquid extraction, extraction and reversed extraction were carried out within the same equipment, the cooling and solvent distillation recovery process are saved, and the technological process is greatly simplified, the required equipment is small, the solvent consumption is also small, the subsequent treatment process is simple, it is low energy consumption, high extraction efficiency, low production cost, and it has higher economic value.

2) **Analysis of economic benefit for three technological processes:** Based on 360 t /day penicillin fermentation broth as example, concentration of penicillin fermentation liquid is 60 000 U/mL, yield of liquid-liquid extraction, DBED and membrane process is 75%,75%, 80% respectively. Comparison of economic cost for 3 processes is listed in Table 1. It can be seen from Table 1, annual output of membrane process can be increased 198 t than the process of liquid-liquid extraction and DBED precipitation, the annual income can be increased by about 18.48 million yuan, if market value is $8 per billion units.

Table 1: Comparison of economic cost (based on 360 t /day penicillin fermentation broth)

material/product	the amount of L-Lextraction process /yield (t)	the amount of DBED precipitation process / yield (t)	the amount of membrane process / yield (t)
60 000 U/mL	360.0	360.0	360.0
extractant loss	13.1-16.3 (butyl acetate)	-	7.0 (7%DOA+ kerosene +30% isooctyl alcohol)
Reversed extract solution	36.0 (2.7M Potassium carbonate solution)	-	140.0 (0.5 M Potassium carbonate solution)
water (only taken into account washing water in the washing process)	36.0	-	0.0
penicillin G	9.8	9.8	10.4

3) Analysis of energy consumption: liquid-liquid extraction process need low temperature operation (less than 10℃)，and a lot of energy were consumed in the cooling process，while the membrane process can be operated at room temperature, energy consumption was reduced, and in the hollow fiber membrane process, there is no need for distillation and purification of the recycled extractant and the solvent in the liquid waste, therefore, the energy consumption in membrane process is greatly reduced. Balance of solvent recovery process by liquid-liquid extraction process is listed in Table 2. It can be seen from Table 2. The energy consumption can be reduced by 5.4×10^4 kJ producing per billion units of penicillin G salt in the membrane process. And about $6 million every year can be saved, meanwhile the solvent recovery process and distillation and purification of waste solvent is eliminated, there is no cooling process , so it can save millions of yuan investment cost.

Table 2: Balance of solvent recovery process by liquid-liquid extraction process(Based on 360 t /day penicillin fermentation broth)

process	heat used/kg
recovery of solvent in the liquid waste	8.6×108
recovery of waste solvent	3.2×107
total	8.9×108

Comments: When appropriate, discuss your results briefly. Comment on what was learned, identify key aspects of the solution, discuss how better results might be obtained by making different design decisions, relaxing certain assumptions, and so on.

In view of this case, firstly, the known conditions: the substance to be separated is penicillin; the background knowledge of penicillin extraction was given. According to the requirements of the subject, the extraction of penicillin is selected by liquid-liquid extraction technology. Then, the students need to consult the relevant literature, according to the properties of penicillin, an effective separation and purification method were be selected and the process routes were designed, and the different process routes were analyzed and compared, which requires not only technical feasibility, but also reflects economic and environmental protection.

Then the key of the design is found: the key to the liquid-liquid extraction process is the selection of extraction solvent. How to choose the suitable extraction solvent? It is necessary to follow the principle: Like Dissolves Like. Organic solvents should also be stable, low toxicity, cheap, easy to recycle and reuse.

After finding the suitable extraction solvent, the process design was carried out. According to the question, three extraction processes of penicillin were designed, respectively: liquid-liquid extraction, DBED precipitation combined with liquid-liquid extraction, and the membrane separating extraction. Then, according to the three extraction processes, the technical analysis, the economic benefit analysis and environmental protection analysis of the process routes were commented, the appropriate process routes were found out through the comparison and selection.

At the end of the case, [1-4] Study Questions are put forward to guide and inspire students' broad thinking and improve their innovative ability.

3. CONCLUSIONS:

Through case teaching, students not only learn to consult technical data, but also design several effective separation and purification methods and process routes according to the property of penicillin, and the established process routes can be analyzed and compared, so that the feasible, economical and optimal technology is found. Students' engineering ability and innovation ability can be improved, and overall concept and consciousness can be cultivated.

Conflicts of Interest: The authors declare no conflict of interest.

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Abbreviations Used:
DBED: Dibenzylethyldiamine

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PICTORIAL ABSTRACT
Design and Origination of Case teaching is as follows.